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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,302	02/08/2001	Rango Dietrich	P66333USO	4778

136 7590 05/27/2005

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 05/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,302	DIETRICH ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Request for Continued Examination (RCE) under 37 CFR 1.114, Applicant's Arguments/Remarks and the request for extension of time (3 months-granted), all filed 02/16/05 is acknowledged.

Claims 21-43 are pending. Claims 1-20 have been cancelled. Claims 21-43 are rejected.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/16/05 has been entered.

Claim Objections

Claim 21 is objected to because of the following informalities:

Claim 21, line 7 recites the phrase '*bears and enteric coating film*'. The term '*and*' should be grammatically corrected to '***an***' instead. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21, 26 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21, 26 and 43 are indefinite because the claim limitation 'a coating film which is customary per se for sustained release compositions' is confusing. Applicant's specification defines the coating film to require the presence of embedded soluble particles or that in which salts are contained (pg.3). It is unclear whether Applicants intend to claim a polymer coating or a polymer coating having the additional ingredients described present. Polymeric coatings are considered to be a film. If Applicants intend to require that the coating film have additional ingredients present (*i.e.* particles, salts), then the term 'customary' should be eliminated and the polymer plus particles or salt claimed. The term 'coating film' is considered to be generic to polymers per se as well as polymers that have particles or salts embedded therein. Clarification is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 21-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dietrich *et al.* (WO 97/02020).

Dietrich *et al.* teach an oral fixed combination pharmaceutical composition containing pantoprazole in pellet or tablet form, wherein the drug is at least partly in slow release form, and is administered in combination with an antimicrobial active (see Abstract); (page 4, lines 15-30). The invention also relates to an oral pharmaceutical composition for treating a disorder caused by Helicobacter comprising pantoprazole in combination with an antimicrobially-active ingredient (pg. 3, lines 1-6). Dietrich *et al.* teach that the compound is pantoprazole, along with its salts and solvates (e.g., hydrates) (pg. 3, 2nd paragraph). According to Dietrich *et al.*, an oral pharmaceutical composition with delayed and controlled release of active ingredients in pellet or tablet form for pantoprazole is provided (pg. 7, 1st paragraph). The invention also provides for an oral pharmaceutical composition in pellet or tablet form for acid-labile irreversible proton pump inhibitors comprising an alkaline pellet or tablet core, at least one release-slowing, release-controlling intermediate layer (for controlled release of the active agent) and an outer enteric

layer, which is soluble in the small intestine, wherein the intermediate layer is formed from a water-insoluble film former. The slowing of release can be achieved, for example by a semi-permeable membrane (pg. 7, lines 18-29). Dietrich *et al.* teach that the pharmaceutical composition can be a combined administration means, being in either *fixed* or free combination administration forms (pg. 4, lines 15-30).

Medicinal dosage forms include, in particular, tablets, coated tablets or pellets, and microtablets in capsules, with the dosage forms designed to achieve and provide for optimal active ingredient profile (pg. 4, line 31 – pg. 5, line 3). A typical dosage for pantoprazole can be regarded as a daily dose of from about 0.01 to about 20 mg/kg of body weight (pg. 5, last paragraph).

Suitable and preferred tablet disintegrants for use in the manufacture of tablet cores include crosslinked polyvinylpyrrolidone (crospovidone), crosslinked sodium carboxymethylcellulose and sodium starch glycolate (pg. 8, last paragraph – pg. 9, line 1).

Film-forming polymers include ethylcellulose, polyvinyl acetate, ammonio methacrylate copolymer type A (e.g., Eudragit® RL) and type B (Eudragit® RS), etc. The release rate can be controlled by incorporating water-soluble pore formers, such as PEG, lactose, mannitol, sorbitol, HPMC, etc and also by the thickness of the coating layer applied (pg. 9, lines 2-10).

Suitable enteric coating polymers include methacrylic acid/methyl methacrylate copolymer or methacrylic acid/ethyl methacrylate copolymer (Eudragit® L) or cellulose derivatives such as carboxymethylethylcellulose (CMEC), cellulose acetate phthalate (CAP), cellulose acetate trimellitate (CAT), hydroxypropylmethylcellulose phthalate (HP50, HPSS), hydroxypropylmethylcellulose acetate succinate (HPMCAS) or polyvinyl acetate phthalate.

Plasticizers (such as propylene glycol), additives and ancillary substances (e.g., buffers, bases, pigments) can also be added (pg. 9, lines 22-32).

Pharmacologically-suitable alkali-metal, alkaline-earth-metal or earth-metal salts of weak acids and the pharmacologically-suitable hydroxides and oxides of alkaline-earth and earth metals are disclosed and include sodium carbonate, for example (page 8, lines 18-26).

Fillers, binders, lubricants, nonstick agents and the like are also disclosed (pg. 8, last paragraph).

The examples at pages 10-14 demonstrate various pantoprazole formulations and methods for preparing thereof.

With regards to the claim limitation 'coating film which is customary per se for sustained release compositions', it is the position of the Examiner that this phrase limitation imparts no unexpected and/or unusual results. The prior art initially recognizes and teaches similar coating films such as those desired by Applicant (*i.e.*, acrylic/methacrylic acid esters) and thus the properties or results imparted by those coating films would also be the same as Applicant's coating film.

Dietrich *et al.* teach an oral pantoprazole fixed combination composition in suitable forms, such as tablets, coated tablets, pellets and microtablets in capsules. The composition provides delayed and controlled release of the active ingredient. Dietrich *et al.* teach tablet disintegrants, film-forming polymers, enteric coatings and various additives. Therefore, it is the position of the Examiner, that given the teachings of Dietrich *et al.*, it would be *prima facie* obvious for one of ordinary skill in the art to use the specific teachings of Dietrich *et al.* who teach a varied release pantoprazole formulation comprising disintegrants, film-forming

polymers, enteric coatings, additives and the like to provide a beneficial drug formulation. The expected result would be an effective formulation in the treatment of various disorders of the stomach.

Claims 21-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen (US Pat. No. 5,260,069) in view of Dietrich *et al.* (WO 97/02020).

Chen teaches a unit dosage form for delivery drugs into the body, wherein a plurality of populations of pellets is provided within a unit dosage form such as a capsule or tablet (see Abstract). The plurality of pellets or particles are completely enclosed within said capsule, each population of pellets constructed to release a drug into said environment of use, whereby all of said pellets are released from said capsule substantially simultaneously, and exposed to the environment when the capsule disintegrates (col. 6, claim 1). Each pellet contains a core including a drug and a swelling agent (col. 6, claim 1). Additionally, each pellet is coated with a coating membrane containing (a) a water insoluble, permeable polymer and one or both of (b) a diffusion controlling agent, and (c) a dissolution controlling agent (col. 3, lines 10-16). The dosage units are readily adaptable to a variety of timing intervals, different therapeutic agents and combination of agents (col. 1, lines 63-68).

Water permeable and insoluble film-forming polymer materials for the coating may include cellulose derivatives, acrylic resins, copolymers of acrylic acid and methacrylic acid esters with quaternary ammonium groups and copolymers of acrylic acid and methacrylic acid esters (col. 3, lines 33-38); (col. 7, claim 7).

Water permeable and soluble film forming agents may include enteric polymers, such as cellulose acetate phthalate, cellulose acetate trimellitate; shellac and methacrylic acid copolymers, such as Eudragit and hydroxypropylmethyl cellulose phthalate (col. 3, lines 48-55); (col. 7, claim 9).

Swelling agents taught include cross-linked polyvinylpyrrolidone (crospovidone), cross-linked carboxymethylcellulose, sodium starch glycolate and pregelatinized starch (col. 3, lines 43-47).

The unit dosage forms taught by Chen include discrete aggregates of populations of pellets contained in capsules, or compressed into tablets or suppositories with binding agents. The dosage form may be arranged to dissolve promptly in any aqueous medium or to resist dissolution in certain environments such as enteric coated tablets which will not release pellets until they have passed the acid stomach and reached the alkaline intestine (col. 5, lines 23-31).

Chen teaches drugs that include antibiotics, tranquilizers, agents acting on the heart, liver, kidney, central nervous system and muscles, contraceptives, hormonal agents, antineoplastic agents and combinations thereof (col. 5, lines 17-22).

The examples at columns 3-5 demonstrate various formulations of multiparticulate, pulsatile unit dosage forms and methods for manufacture thereof.

Chen teaches that the formulation can be used with a variety of active agents including water-soluble as well as water-insoluble drugs or combination of drugs (col. 3, lines 31-32); (col. 5, lines 17-22). Chen does not teach the drug to be a benzimidazole. It is deemed obvious to one of ordinary skill in the art to employ any particular active ingredient, based on the intended or desired purpose.

Dietrich *et al.* (WO 97/02020) teach an oral fixed combination pharmaceutical composition containing pantoprazole in pellet or tablet form, wherein the drug is at least partly in slow release form, and is administered in combination with an antimicrobial active (see Abstract); (page 4, lines 15-30). The oral pharmaceutical composition provides for the delayed and controlled release of active ingredients in pellet or tablet form for pantoprazole (pg. 7, 1st paragraph). The composition in pellet or tablet form for acid-labile irreversible proton pump inhibitors comprises an alkaline pellet or tablet core, at least one release-slowing, release-controlling intermediate layer (for controlled release of the active agent) and an outer enteric layer, which is soluble in the small intestine, wherein the intermediate layer is formed from a water-insoluble film former.

It is the position of the Examiner that one of ordinary skill in the art would have been motivated to combine the teachings of Dietrich *et al.* within Chen. Chen teaches a dosage form comprising a capsule containing pellets with varying rates of release of the active ingredient. While Chen does not teach the active ingredient to be a benzimidazole, Dietrich *et al.* teach pantoprazole as the preferred active ingredient to treat disorders of the stomach and teach the pantoprazole in a varied or distinct release oral composition.

Therefore, it would be *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the combined teachings of Dietrich *et al.* within Chen to obtain suitable formulations of a benzimidazole, particularly pantoprazole for treating gastric acid conditions. The expected result would be a highly effective pantoprazole composition, which is beneficial for treating disorders of the stomach, as similarly desired by Applicants.

Response to Arguments

Applicant's arguments filed 2/16/05 have been fully considered but they are not persuasive.

Applicant argued "The references cited by the Examiner do not suggest all features of the administration form according to their invention based on (1) an enteric coated form and (2) a non-enteric coated form, which has a coating which is customary per se for sustained release compositions, which only releases the benzimidazole after gastric passage. The release of active compounds according to Applicant's invention is not at two different points in time. The applied prior art provides no motivation to combine any particular limitations disclosed in the prior art."

Applicants' arguments have been fully considered but were not found to be persuasive. The prior art provides ample motivation to arrive at the presently claimed invention. The prior art teaches enteric and non-enteric coated pantoprazole formulations for treating stomach disorders and teaches that it is known in the art to coat tablets or pellets which contain acid-labile active ingredients with enteric coatings, which 'after passage through the stomach' rapidly dissolves in the alkaline medium in the intestine (see pg. 6, 1st paragraph of Dietrich et al.). Applicants' argument that the prior art does not teach a coating 'which is customary per se for sustained release compositions' is not persuasive since the prior art teaches the inclusion of the same coatings (*i.e.*, cellulose ethers/esters & copolymers of acrylic/methacrylic acid esters) desired by Applicant and therefore, the results, properties and characteristics imparted by those particular coatings would also be the same (see Dietrich et al. pg. 9, 4th paragraph and Chen col. 3, lines 33-37). The prior art teaches a formulation comprising the same ingredients (*i.e.*, pantoprazole), used in the same field of endeavor to treat the same problems (gastric acid

disorders) as Applicant, therefore, the instant invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

H. N. Sheikh H. N. Sheikh

Patent Examiner

Art Unit 1615

May 25, 2005